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ML, MR, NE, SN, TD, TG).

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- with international search report
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15 September 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: TARGETS FOR TUMOR GROWTH INHIBITION

(57) Abstract: The present invention relates to methods for treating cancers by manipulating a target gene expression by up-regulation, silencing and/or down-regulation of the gene, such as EGFR-RP, TRA1, MFGE8, TNFSF13 and ZFP236, respectively. The methods are useful in treating cancers and/or inhibiting tumor growth by enhancing expression of a gene that is validated as a target such as ICT1030, for protein, peptide drug and gene therapy modalities; or by RNA interference to silence and/or down-regulate targets such as ICT1024, ICT1025 and ICT1031 and ICB1003 that are validated for antibody, small molecule and other inhibitor drug modalities.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 48/00; C07H 21/04

US CL : 514/44; 536/23.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. :

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,309,636 (DO COUTO et al.) 30 October 2001 (30.10.2001), see entire document	1-32

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

08 July 2005 (08.07.2005)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



in written format



in computer readable form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in computer readable form



furnished subsequently to this Authority for the purposes of search

2. ☒

In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-32 and SEQ ID NOS: 1-3

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-32, drawn to a method of treating a disease associated with ICT1030 peptide in a mammal using a composition that enhances expression or activity of ICT1030.

Group 2, claim(s) 33-47 and 57-73, drawn to a method of treating a disease associated with ICT1031 peptide in a mammal using a composition that reduces expression or activity of ICT1031.

Group 3, claim(s) 33-43, 51-53 and 57-73, drawn to a method of treating a disease associated with ICT1024 peptide in a mammal using a composition that reduces expression or activity of ICT1024.

Group 4, claim(s) 33-43 and 54-73, drawn to a method of treating a disease associated with ICT1025 peptide in a mammal using a composition that reduces expression or activity of ICT1025.

Group 5, claim(s) 33-43, 48-50 and 57-73, drawn to a method of treating a disease associated with ICT1003 peptide in a mammal using a composition that reduces expression or activity of ICT1003.

The inventions listed as Groups 1-5 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group 4 is directed to use of a composition that interacts with ICT1025. The composition may be a nucleic acid that is provided as a vector. ICT1025 is also known as the glucose related protein GRP94. Nucleic acids that interact with GRP94 are not a contribution over the prior art. See for example REDDY et al. (The Endoplasmic Reticulum Chaperone Glycoprotein GRP94 with Ca²⁺-binding and Antiapoptotic Properties is a Novel Proteolytic Target of Calpain during Etoposide-induced Apoptosis, *Journal of Biological Chemistry* 1999, Vol. 274, No. 40, pages 28476-28483). Reddy et al. disclose a vector containing an antisense sequence of GRP94. This vector was used to reduce the amount of GRP94 in Jurkat cells, demonstrating that this vector is a nucleic acid that interacts with ICT1025.

Further, according to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the target peptides listed in claim 33, the Markush group shall be regarded as being of similar nature when:

- (A) all alternatives have a common property or activity and
- (B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or
- (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant target peptides are considered to be each separate inventions for the following reasons:

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The target peptides do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. Each of the different target peptides is a unique protein that belongs to a different class of proteins and has a different function. For example, ICT 1030 is also known as breast epithelial BA46 antigen, ICT 1031 is one of the proteins in the TNF ligand super family, ICT 1024 is also known as EGF receptor-related protein, a membrane protein and ICT 1025 is also known as tumor rejection antigen, which is involved with antigen presentation. Each member of the class cannot be substituted, one for the other.

Further, the instant peptides do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure due to their unique amino acid sequence. Accordingly, unity of invention between the target peptides of the instant application is lacking and each target peptide is considered to constitute a special technical feature.

The special technical feature of group 1 is a composition that interacts with ICT1030.

The special technical feature of group 2 is a composition that interacts with ICT1031.

The special technical feature of group 3 is a composition that interacts with of ICT1024.

The special technical feature of group 4 is a composition that interacts with of ICT1025.

The special technical feature of group 5 is a composition that interacts with ICT1003.

Continuation of B. FIELDS SEARCHED Item 3:

EAST, STN: mfge8, milk fat globule egf factor 8, ba46, lactadherin, increase or enhance expression, cancer, disease

STIC: sequence search of SEQ ID NOS: 1-3